Remarks

Restriction Requirement

Claims 48-72 are pending in the application. The Examiner has required a restriction of the application to claims in one of the following groups:

Group I: Claims 48-59, drawn to a method for producing glucocerebrosidase from a culture of mammalian cells, classified in class 435, subclass 70.1.

Group II: Claims 60-66, drawn to a composition comprising glucocerebrosidase containing a higher number of exposed mannose residues than human placental glucocerebrosidase, classified in class 435, subclass 200.

Group III: Claims 67-72, drawn to a method of treating a human patient having Gaucher's disease comprising administering a composition comprising glucocerebrosidase containing a higher number of exposed mannose residues than human placental glucocerebrosidase, classified in class 424, subclass 94.61.

Applicants respectfully submit that the restriction is improper and should be withdrawn. Accordingly, Applicants traverse.

The claims of Group I are drawn to a method for producing glucocerebrosidase "useful for the treatment of a human patient having Gaucher's disease," which method requires, *inter alia,* treating cultured mammalian cells capable of expressing glucocerebrosidase with "an inhibitor of carbohydrate processing that acts to inhibit the conversion of $Glc_3Man_9GlcNac_2$ to smaller species" so as to produce glucocerebrosidase containing a higher number of exposed mannose residues than human placental glucocerebrosidase. The claims of Group II are drawn to a pharmaceutical composition "useful for the treatment of a human patient having Gaucher's disease" comprising glucocerebrosidase "produced by treating cells expressing glucocerebrosidase with an inhibitor of carbohydrate processing that acts to inhibit the conversion of $Glc_3Man_9GlcNac_2$ to smaller species." The claims of Group III are drawn to a "method

of treating a human patient having Gaucher's disease" comprising administering a composition according the claims of Group II.

The Examiner states that the claims of Groups I and II are distinct because "the product made [glucocerebrosidase] can be made by any method of protein synthesis, such as chemical synthesis or expression in non-mammalian cells, with the exposed mannose residues added *in vitro*." The Examiner is mistaken. According to the composition claims of Group II, the glucocerebrosidase must be produced by treating cells expressing glucocerebrosidase in the same manner as described in the process claims of Group I. Specifically, the claims in both groups require treating cells expressing glucocerebrosidase with an inhibitor of carbohydrate processing that acts to inhibit the conversion of Glc_3 $Man_9GlcNac_2$ to smaller species.

The Examiner further states that the claims of Groups II and III are distinct because "the glucocerebrosidase can be used in processes other than a method of treatment. For example, ... as a standard in an assay." Again, the Examiner is mistaken. All of the claims of Group II specifically recite that the glucocerebrosidase or the composition comprising it is "useful for the treatment of human patient having Gaucher's disease." Furthermore, all of the method of treatment claims of Group III are limited to a method of treating a human patient having Gaucher's disease by administering a composition according to the claims of Group II. Finally, the Examiner's position that the glucocerebrosidase can be used as a standard in an assay is not consistent with the claims of Group II, which are directed to a *pharmaceutical* composition or a composition "useful for the treatment of a human patient having Gaucher's disease."

Finally, the Examiner contends that the claims of Group I and Group III are directed to distinct methods because the claims of Group III comprises "steps, such as administering a composition comprising a glucocerebrosidase to a patient having Gaucher's disease, that are not comprised in the method of Group I." The Examiner has apparently overlooked the fact that all of the claims of Group I specifically recite a method for producing glucocerebrosidase "useful for the treatment of a human patient having Gaucher's disease...." Furthermore, the claims of both Group I and Group III involve glucocerebrosidase containing a higher number of exposed mannose residues than human placental glucocerebrosidase, which glucocerebrosidase is produced by

treating cells capable of expressing glucocerebrosidase with an inhibitor of carbohydrate processing that acts to inhibit the conversion of $Glc_3Man_9GlcNac_2$ to smaller species.

In view of the above, applicants submit that the claims of Groups I, II and III do not represent distinct inventions. Accordingly, Applicants respectfully request the Requirement for Restriction be withdrawn.

In the event the Examiner nevertheless disagrees, Applicants elect, with traverse, Group I, corresponding to claims 48-59. Applicants reserve the right to file related applications directed to the subject matter of the non-elected claims.

Species Election

The Examiner states that the product claims of Group II and the method claims of Group I and III are directed to the following patentably distinct species of inhibitors of carbohydrate processing: deoxy-mannojirimycin, swainsonine, castanospermine, deoxy-nojirimycin and N-methyl-deoxy-nojirimycin. Specifically, the Examiner asserts that Applicants must elect a single disclosed species for prosecution because, "[a]bsent evidence to the contrary, each of the distinct inhibitors of carbohydrate processing would produce a glucocerebrosidase comprising a different pattern of glycosylation and, therefore, having distinct structural and functional properties."

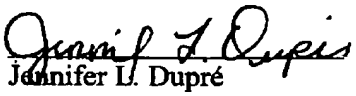
Applicants respectfully submit that the Examiner has presented no evidence to support his assertion that these inhibitors of carbohydrate processing, all of which act to inhibit the conversion of $Glc_3Man_9GlcNac_2$ to smaller species, would produce glucocerebrosidase having distinct structural and functional properties. In fact, Applicants believe that the claimed inhibitors of carbohydrate processing all produce glucocerebrosidase with similar functional characteristics -- they all produce glucocerebrosidase with improved binding to mannose receptors. In addition, carbohydrate processing inhibitors are interrelated and a search of one inhibitor of carbohydrate processing would likely include a search of other inhibitors of carbohydrate processing and would not result in an undue burden on the Examiner. Thus, Applicants request that the requirement for species election be withdrawn. Nevertheless, in the event the Examiner declines to withdraw the requirement, Applicants elect, with traverse, the species "deoxy-mannojirimycin." Applicants reserve the right to file related

applications directed to the subject matter of the non-elected claims.

Applicants request reconsideration and withdrawal of the requirements for restriction and election in view of the foregoing remarks. If the Examiner believes that a conversation with the Applicants' attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned.

Respectfully submitted,

Date: June 1, 2005



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